REMARKS/ARGUMENTS

Status of the claims

Claims 1, 3, 5, and 11 are pending. Claim 1 is amended to incorporate the limitations of claim 13, which is now canceled. No new matter is added.

September 1, 2010 Interview

Applicants' representative, Carol Johns, appreciates the opportunity to discuss the pending rejections with Bao Li and Zach Lucas during the September 1, 2010 interview

Specification

The Examiner has objected to the specification as allegedly describing "Felidovac PCR" instead of "Felidovac PRC," which the Examiner asserts is correct. The Examiner further requests that the specification be amended to add a trademark if appropriate, and the components of Felidovac (Office Action, pages 9-10). Solely in an effort to expedite prosecution, Applicants have amended paragraph 242 (page 42 of the specification as filed) to indicate that Felidovac is, indeed, a trademark. Support for the amendment is found in **Exhibits A** and **B**, a copy of the entry from the Trademark Electronic Search System (TESS) and a copy of the package insert in Japanese, respectively (see bolded characters followed by "® PCR" at the top of the first page of **Ex. B**).

Applicants were not able to access the website cited by the Examiner to support the alleged inaccuracy of the term "Felidovac PCR," that is, http://stjankatten.se/art. Applicants note that the printout provided with the Office Action represents a Google translation. In support of the term "Felidovac® PCR," Applicants point to **Ex. B** and page 34 of Hohdatsu *et al.* (2003) *Vet. Microbiol.* 97:31, which was submitted with the amendment of April 13, 2009, and is submitted herewith as **Exhibit C**. **Ex. C** represents a peer-reviewed publication where inaccuracies are subject to editorial correction.

Regarding the components of the adjuvant mixture described in amended paragraph 242, Applicants respectfully submit that the description of Felidovac® PCR in the specification meets the requirements set forth in the MPEP.

Proper identification of a trademarked product is addressed in MPEP 608.01(v). The section explains that a trademark must be distinguished from common descriptive nouns by capitalization. If the trademark has a fixed and definite meaning, it constitutes sufficient identification unless some physical or chemical characteristic of the article or material is involved in the invention.

The claims recite "one or more adjuvants," not "Felidovac® PCR." The adjuvant components of Felidovac® PCR are described in the specification, that is, L80 and aluminum hydroxide.

Felidovac® PCR is a trademarked product and has a fixed definition, as evidenced by the package insert, **Ex. B**. As amended, paragraph 242 refers to Felidovac® PCR (capitalized and marked), and describes it in common terms, *i.e.*, a feline inactivated trivalent vaccine with Adjuvant L80 and aluminum hydroxide. Thus, to the extent that L80 and aluminum hydroxide can be involved in the invention as "one or more adjuvants," these are set forth. For the record, Applicants submit **Exhibit D**, a translation from the inventors of the component list in **Ex. B**. **Ex. B** and **D** confirm that L80 and aluminum hydroxide are included in the trivalent vaccine.

This issue is addressed in more detail in the arguments for enablement, below. In brief, one of skill would be enabled to select an appropriate adjuvant for the claimed vaccines. Adjuvants and their uses were well-known at the time of the invention, and the data in the specification show that the non-adjuvant components of Felidovac® PCR do not confer protection from FIPV. The non-adjuvant components of Felidovac® PCR are not involved in the invention, and thus need not be included in the specification.

Moreover, Felidovac® PCR has a fixed definition. Thus, the description of the single 2 mL dose in amended paragraph 242, which includes 1 mL of Felidovac® PCR, can be understood by one of skill in the art.

In view of the foregoing, Applicants respectfully request withdrawal of the objections to the specification.

Rejection under 35 USC § 112, first paragraph – Written Description

The Examiner has maintained the rejection of claims 1 and 5 as allegedly lacking written description. Solely in an effort to expedite prosecution, claim 1 is amended to include the limitation of claim13. Claim 5 depends on claim 1. In view of the amendment to the claim, Applicants respectfully request withdrawal of the rejection under the first paragraph of 35 USC § 112 for written description.

Rejection under 35 USC § 103

The Examiner has maintained the rejection of claims 1 and 3 as allegedly obvious over Wasmoen (US Patent No. 5770211) in view of Motokawa *et al.* (1996) *Microbiol. Immunol.* 40:425 and Duphar (EP0411684), as further substantiated by Wasmoen *et al.* (1995) *Adv. Exp. Biol.* 380:221. According to the Examiner, the Applicants' earlier arguments were considered persuasive (Office Action, page 6, paragraph 19). The Examiner then states that "the polypeptide N from type I FIPV had been completely disclose, and the method for using a N protein as an immunogenic polypeptide … had been taught," so "it would have been obvious for using the N protein of type II FIPV in combination with an adjuvant to make an immunogenic composition" (Office Action, page 6, paragraph 20).

This rejection was discussed during the September 1, 2010 interview. Applicants again explained that *the claims are **not** directed to use of N protein from a **type II FIPV**.* The claims ***are** directed to use of N protein from a **type I FIPV**,* which was not expected to give rise to a immunogenic response. The cited art discloses the sequence of N protein from a type I FIPV, and use of a type II FIPV N protein, an immunogenically distinct entity, in a live raccoon poxvirus vaccine. Not only has the Examiner failed to establish a reasonable expectation of success using a type I FIPV N protein, but the claimed invention provides secondary considerations such as unexpected results and failure of others. These arguments are set forth in detail on pages 6-11 of the May 14, 2010 amendment, along with objective supporting evidence.

Moreover, the rationale given for the obviousness rejection contradicts the rejection under the first paragraph of 35 USC § 112 for enablement (addressed below). That is, while the Examiner alleges that it would be obvious to combine a type II (sic) N protein with an adjuvant to make an immunogenic composition, the Examiner also alleges that the specification fails to enable use of a variant of the polypeptide of SEQ ID NO:2 with any vaccine adjuvant.

As explained on page 11 of the amendment submitted May 14, 2010, a claimed invention cannot be both obvious and non-enabled. To be obvious, the prior art, *even without the benefit of an applicant's disclosure*, must teach one of skill how to practice the invention. To not be enabled, the application, in combination with the prior art, must *not* sufficiently teach one of skill how to practice the invention.

Agreement was reached during the interview that the rejection under 35 USC § 103 should be withdrawn. In view of the foregoing comments, Applicants respectfully request withdrawal of the obviousness rejection.

Rejection under 35 USC § 112, first paragraph - Enablement

The Examiner has rejected claims 1, 3, 5, 11, and 13 as allegedly lacking enablement. As noted above, the Examiner alleges that the specification fails to enable use of a variant of the polypeptide of SEQ ID NO:2 with any vaccine adjuvant. According to the Examiner, the specification enables use of SEQ ID NO:2 with an adjuvant comprising L80, aluminum hydroxide, and feline inactivated trivalent vaccine (Office Action, page 7). Thus, the Examiner objects to two aspects of un-amended claim 1: (1) the identity of the immunogenic polypeptide and (2) the identity of the adjuvant.

Identity of the polypeptide

Regarding the identity of the polypeptide, solely in an effort to expedite prosecution, claim 1 is amended to describe the immunogenic polypeptide as comprising the amino acid sequence of SEQ ID NO:2, or an immunostimulating fragment having 45 or more continuous amino acids of SEQ ID NO:2.

Identity of the adjuvant

The rejection relating to the adjuvant is set forth primarily on pages 8-9, in paragraph 30 of the Office Action. The Examiner states that different ***antigens*** are capable of inducing different immune response (sic). The Examiner states that there are many types of adjuvants in the art as evidenced by Cox, and asserts that some are good for Th1 or Th2 type immune response. The Examiner then states that Hebben teach that different ***antigen proteins*** of FIPV can induce different (Th1 or Th2) immune responses. The Examiner asserts that expression of FIPV ***antigen proteins*** from the modified vaccinia virus Ankara (MVA) expression vector discussed in Hebben induces a better immune response because it keeps a better Th1/Th2 immune response balance.

From these statements, the Examiner concludes that selection of an appropriate adjuvant to boost the right type of immune response is very important. The Examiner further concludes that an impropriate (sic) adjuvant may cause suppress (sic) the right immune response and potentiate a wrong immune response.

The MPEP 2164.04 states that the burden for providing a *reasonable* explanation as to why the scope of a claim is not adequately enabled by the disclosure. The explanation can be established based on "findings of fact, supported by the evidence, and ...conclusions based on these findings of fact." This section moreover cautions against limiting claim scope to less than the broadest reasonable interpretation.

> To demand that the first to disclose shall limit his claims to what he has found will work or to materials which meet the guidelines specified for "preferred" materials in a process such as the one herein involved would not serve the constitutional purpose of promoting progress in the useful arts. MPEP 2164.04.

Applicants respectfully traverse the rejection as it relates to the identity of the adjuvant. Applicants are the first to disclose that a protein antigen from a type I FIPV N protein can successfully protect cats from exposure to live FIPV virus. In making the present rejection, the Examiner has set forth statements supporting the importance of ***antigen*** selection, and provided a disclosure showing that adjuvants were well known in the art at the time of the invention.

Applicants agree that selection of the right ***antigen*** can be important in determining the type of immune response that will result. While not directly on point, Hebben shows that the *amount* (expression level) of the selected antigen can be important for the immunogenicity of a virally-expressed FIPV antigen. The modified viral vector described in Hebben was designed to drive expression during both early and late stages of the MVA viral vector, instead of during the early stage only. The increased amount and duration of FIPV antigen expression resulted in improved immunogenicity. Hebben does not describe use of an adjuvant. The term does not appear in Hebben.

Applicants also agree that there are many types of adjuvants. Indeed, Cox shows that, as of 1992, the art was very familiar with adjuvants, and with the selection of the appropriate type of adjuvant to produce the desired immune response.

Cox defines an adjuvant as a substance that results in a specific increase in the immunogenicity of a vaccine component (Cox, bottom of page 52). Cox, published 10 years before the priority date of the present application, goes on to review dozens of adjuvants and adjuvant combinations that can be used for particular purposes. Cox supports the contention on page 21 of the specification (copied below) that one of skill can select an appropriate adjuvant for a desired response from well-characterized possibilities. Experimentation may be required, but such experimentation would hardly be considered undue for one familiar with vaccine design.

> Adjuvants may be used alone or in combination with a number of substances. Vaccine specialists can determine appropriate adjuvant combinations by experimentation. Depending on the type of adjuvant, those that mainly stimulate humoral immunity, and those that mainly stimulate cellular immunity are known. For example, aluminum phosphate is known as an adjuvant that mainly stimulates humoral immunity. On the other hand, saponins such as Quil A and QS-21, pertussis toxin, cholera toxin, and such are known to easily stimulate cellular immunity. Adjuvants appropriate for use in combination with particular antigens can be selected while referring to such information.

Applicants now turn to the data presented in the specification, for example, on page 45. In brief, 75% of the cats vaccinated with the FIPV type I N protein antigen combined

with the adjuvant combination described on page 42 of the specification survived challenge with a live virus. In marked contrast, 100% of the cats vaccinated with the control SF-9 cell precipitate combined with the adjuvant combination described on page 42 of the specification died. The one cat that was treated with type I N protein antigen but did not survive the challenge demonstrated longer post-challenge survival (48 days) than the control cats (23-44 days).

Similar results were observed in the vaccination and challenge described on page 52 of the specification.

Thus, the protective effect shown in the present disclosure is due to the FIPV type I N protein antigen, ***not*** the vaccine components of the Felidovac® PCR used in the disclosed examples. The data show that cats vaccinated with non-specific SF-9 cell precipitate + adjuvant (*i.e.*, Felidovac®, including aluminum hydroxide and L80) **do not survive** challenge from live FIPV. Conversely, cats vaccinated with FIPV type I N protein antigen + adjuvant (Felidovac®, including aluminum hydroxide and L80) show at the very least an increased time of survival, if not complete survival.

Yet despite the fact that adjuvants and their activities were well known at the time of the invention, and evidence that the protective effect of the claimed vaccines is not due to the adjuvant, the Examiner has alleged that a Ph.D. in immunology or virology would face undue experimentation selecting an adjuvant (Office Action page 10, paragraph 32). The rejection improperly seeks to limit the scope of the claims to the disclosed example. Following the Examiner's reasoning, to be enabling for use of "one or more adjuvants," the specification would have to provide *in vivo* data showing the effectiveness of every adjuvant and adjuvant combination known in the art to improve cellular immune responses. This simply cannot be required for enablement.

The Examiner has alleged that the specification is not enabled for use of an adjuvant other than the one used for generating the ***in vivo*** data, despite the general description of adjuvants on pages 20-21 of the specification, and the extensive knowledge in the field at the time of the invention. Instead of a reasonable explanation, the Examiner has based the allegation on evidence showing that antigen selection can be important in determining the type of immune response, and that many adjuvants were known at the time. Finally, the data disclosed in the

specification show that the recited FIPV type I N polypeptide is required for conferring protection from a challenge with live FIPV; adjuvant alone (Felidovac®, including aluminum hydroxide and L80) is not sufficient.

Applicants were the first to disclose the successful use of an FIPV type I N protein in a vaccine, and this fact has been recognized by experts in the field (*see, e.g.*, Horzinek, submitted with the April 13, 2009 response). The inventors selected a particular adjuvant mixture to use with their antigen in the set of "proof of concept" examples disclosed in the specification. Yet limiting the claims to this exemplary adjuvant mixture would render the value of the inventors' contribution insignificant. This is especially true given the familiarity of the art with adjuvants. In view of the foregoing comments, Applicants respectfully request withdrawal of the rejection under the first paragraph of 35 USC § 112 for enablement.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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